REMARKS

Status of the Claims

Claims 25, 29-31, 35-37, 41 and 42 are pending in the application. In the present Amendment, claims 25, 29, 30, 31, 36, 37, and 42 have been amended. Claims 26, 27, 28, 32, 33, 34, 38, 39 and 40 has been canceled. Applicants have not introduced any new matter by the amendments, nor are any estoppels intended thereby. Further, the amendments do not raise new issues or necessitate the undertaking of any additional search of the art by the Examiner.

Rejection Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 30, 36 and 42 under 35 U.S.C. § 112, second paragraph, as being indefinite since monoclonal antibodies, per se, are not "natural." Office Action, page 2. Applicants respectively traverse this rejection.

However, in an effort to expedite prosecution, Applicants have amended the claims to remove this language. Applicants therefore request that these rejections be withdrawn.

Rejection Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 25-42 under 35 U.S.C. § 112, first paragraph, because while being enabling for the monoclonal antibody 16C2 that binds VASP as antigen when VASP is present in the phosphorylated form, does not reasonable provide enablement for any other antigen binding protein nor any other monoclonal antibody

which recognizes VASP as antigen when VASP is present in the phosphorylated form. Office Action, pages 2-3. Applicants respectively traverse this rejection.

However, solely in an effort to expedite prosecution, Applicants have amended the instant claims to an antigen binding protein which recognizes VASP as antigen only when VASP is present in phosphorylated form, and wherein the VASP is phosphorylated at position serine 157 or wherein the VASP is phosphorylated at position serine 239. The claims as amended are clearly enabled.

Regarding an antigen binding protein that recognizes VASP as antigen only when VASP is present in phosphorylated form, and wherein the VASP is phosphorylated at position serine 157, Applicants respectfully submit that the instant specification provides sufficient disclosure to generate and isolate monoclonal antibodies which are specific for VASP when it is phosphorylated at position serine 157.

For example, the specification teaches on page 10, lines 17 to lines 26 that a peptide that is phosphorylated at position serine 157 and is about 6 to about 12 amino acids long can be used for immunization. To demonstrate, Example 1 is attached showing the generation of the antibody 5C6, the peptide (phosphorylated at serine 157) ERRS^{157} NAG, *i.e.* a peptide with a length of 7 amino acids. Thereafter, the immunization protocol, the screening protocol for antibodies that are specific for VASP when phosphorylated at position serine 157 and the isolation of these antibodies are the same that have been described on page 19 to 21 of the original application for the generation and isolation of the monoclonal antibody 16C2.

More specifically, on page 21, lines 3 to 7 of the instant specification, it states that the antibodies specific for VASP when phosphorylated at position serine 157 can

be isolated with the method described for the antibody 16C2 "by employing sequences around serine 157 of the VASP protein as the antigen". Applicants submit two publications in the accompanying Information Disclosure Statement, Smolenski et al., (2000), J. Biol. Chem., 275: 25723-25732, and Burkhardt et al. (2000), J. Biol. Chem. 275: 33536-33542, that demonstrate that this is effective. For example, the antibody 5C6 is specific for Ser 157 in its phosphorylated state (see, for example, Smolenski et al, paragraph bridging columns on page 57252). Both publications clearly state "that the antibody 5C6 was prepared by the present inventors by the same approach used for making the antibody 16C2 (see Smolenski et al, page 25724, left column, section "experimental procedures" and corresponding footnote, Burkhardt et al., page 33537, left column, section "experimental procedures" and corresponding footnote).

Accordingly, the originally filed specification provides sufficient disclosure to prepare monoclonal antibodies that are specific for VASP having Ser 157 in its phosphorylated state.

Regarding monoclonal antibodies that bind VASP specifically when Ser 239 is in its phosphorylated state, Applicants have submitted attached Example 2. The example demonstrates that three monoclonal antibodies (pS239)-22E11B8, (pS239)-22E11D3 and (pS239)-22E11G10 have been generated and isolated as described in the original PCT application for the antibody 16C2. In addition, when comparing these antibodies to the antibody 16C2 (that is explicitly described in the present application) in a test similar to the one described in Example 5 of the present application (see page 23 of the published PCT application), Example 2 shows that the three monoclonal antibodies (pS239)-22E11B8, (pS239)-22E11D3 and (pS239)-22E11G10 only recognize VASP

when this protein is phosphorylated at the position serine 239 and have a sensitity comparable to the one of the antibody 16C2.

The test for enablement is whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976). An enablement inquiry considers, but is not limited to, the following factors: (A) the breath of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988); *see also*, M.P.E.P. 2164.01(a). The Office's analysis, however, must consider all the evidence related to each of these factors and any conclusions of nonenablement must be based on the evidence as a whole. *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404, 1407 (Fed. Cir. 1988). Further, specific technical reasons are always required to support a prima facie case of lack of enablement. M.P.E.P. 2164.04.

As outlined above, the instant specification provides ample direction regarding the invention as now claimed. If the Office maintains this rejection, it must establish technical reasons to question the enablement in view of the above evidence.

In view of the above remarks, Applicants respectfully request that these rejections be withdrawn.

Rejection Under 35 U.S.C. § 102

The Examiner has rejected Claims 25, 27, 29-31, 33, 35-37, 39, 41 and 42 as being clearly anticipated by *Abel et al*, (Eur. J. Cell Biol. 1996). According to the

Examiner, *Abel* discloses VASP phosphorylation/dephosphorylation monoclonal antibodies and states that a monoclonal antibody was found to inhibit phosphorylation and dephosphorylation of VASP at Ser^{157}. Office action, page 4. Applicants respectfully traverse.

The instant amendments clarify that the claims are directed to an antigen binding protein which binds VASP (vasodilator-stimulated phosphoprotein) as antigen **only** when VASP is present in phosphorylated form. *Abel* describes monoclonal antibodies, which recognize the VASP protein **independently** of its phosphorylation status. As the Examiner correctly states, the *Abel* antibodies inhibit phosphorylation and de-phosphorylation of VASP by the respective protein kinases by steric hindrance, but they do not recognize phosphorylated VASP. Office Action, page 4.

Therefore, the antigen binding protein of the amended claims, which binds VASP as antigen **only** when VASP is present in phosphorylated form, is not disclosed by *Abel*. Therefore, Applicants respectfully request that this rejection be withdrawn.

If there is any fee due in connection with the filing of this Amendment, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

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